THE TRANSMISSION OF SPECIFIC IMMUNE BODIES FROM THE MOTHER TO THE YOUNG

KATHARINE M. HOWELL AND HARRIET EBY

From the Nelson Morris Memorial Institute for Medical Research of the Michael Reese Hospital, Chicago

The earlier literature relating to the transfer of antibodies from the mother to the offspring was reviewed by Morgenroth.[1] He discussed the four possibilities of the transmission of immunity: (1) the direct transmission of the newly acquired immune factor of the parents to the germ plasma (true inheritance); (2) the active immunization of mother and fetus by the same immunizing factor; (3) the passive immunity of the fetus by circulating antibodies in the mother's blood; and (4) the transmission of antibodies through the mother's milk. He concluded from the detailed experiments of Ehrlich and others that there was no actual inheritance of immunity, and that the immunity which occurred in the young of immune mothers depended partially on the intra-uterine transfer of maternal antibodies in the circulation of the fetus and partially on the transmission of antibodies through the mother's milk. In most of the earlier work on the transmission of immunity, toxins were the immunizing agents of choice, although bacteria and lysins were used to some extent. The results of the experimental work reviewed by Morgenroth were conflicting, as are those of today. Reymann,[2] for example, in his recent review of the literature on the transmission of agglutinins from mother to young, states that the majority of investigators have concluded that agglutinin was absent or less in amount in the blood of the offspring than in that of the mother, but that some investigators have found even more antibodies in the offspring's blood than in the mother's. Reymann concluded from his own experiments that the antibody content in the blood of the offspring was in some cases more and in others less than in that of the mother, and in some cases transmission by the mother's milk appeared probable. Tunnicliff,[3] in a review of the observations that had been made on the transmission of opsonins, found that the same contradictory conclusions existed as in the case of agglutinins. Tunnicliff's experiments showed that the opsonic power of serum for various bacteria was less at birth than in adult life, and that opsonins decreased during the first month of life. Eisler and Sohma[4] found that normal opsonin was transmitted from a normal mother to her offspring, but that immune opsonin was not transferred from an immunized mother to her young.

The following experiments dealt with (1) the effects of parturition on the antibody content of the serum of an immune rabbit, (2) the antibody content of the serum of the offspring of an immune rabbit, and (3) the duration of immune bodies in the serum of the offspring of immune rabbits.

Six rabbits, before pregnancy, were immunized for the antibody test. Two rabbits were immunized against red blood cells; rabbit 1 against human corpuscles and rabbit 2 against sheep corpuscles. Four rabbits were immunized against bacteria; rabbit 3 against Streptococcus viridans, rabbit 4 against type 2 pneumococcus, rabbit 5 against meningococcus, and rabbit 6 against

Received for publication Aug. 21, 1920.

1 Kolle u. Wassermann Handbuch d. path. Mikroorg., 1904, 4, p. 784.
2 Jour. of Immunology, 1920, 5, p. 227.
3 Jour. Infect. Dis., 1910, 7, p. 698.
4 Wien. klin. Wchnschr., 1908, 21, p. 684.

B. typhosus. A high degree of immunity was maintained by a weekly injection of the immunizing agent during pregnancy. Immunization was discontinued after parturition. The blood of both mother and offspring was tested for antibody content as soon after parturition as possible. It was feared that the young rabbits might not survive a bleeding from the heart, and since it was desirable to keep the offspring of each immune rabbit under observation for some weeks, only one rabbit was bled at a time until they were several weeks old. The serum from 2 rabbits and their young was examined for hemolytic amboceptor, serum from 4 rabbits and their offspring for bacterial complement fixation bodies, serum from 2 rabbits and their offspring for bacterial agglutinin, and serum from 1 rabbit and its young for opsonin.

The following technic was used for the tests: Serum inactivated by heating at 56 C. for 1 hour was used in all the tests. A normal serum was used in each test as a control for the immune serums. Hemolytic amboceptor was titrated by the usual method—to varying dilutions of inactivated immune serum 2 units of complement and a 5% homologous corpuscle suspension were added. The test was incubated at 37 C. for 2 hours, and the highest dilution of serum completely laking the corpuscles was noted. The figures given in table 1 and table 2 represent this dilution.

Complement-Fixation Antibodies.—The bacterial complement-fixation tests were made according to the original Wassermann test (one-tenth method). The antigens used in the tests were heated bacterial suspensions in normal salt solution. When there was complete inhibition of hemolysis with ¼ and ⅛ of the anticomplementary unit of antigen, the test was considered weakly positive and was indicated in the table by +. Fixation with 1/16 and 1/32 was indicated by + +, fixation with 1/64 and 1/128, by + + +, and fixation with 1/256 or over, by + + + +.

Agglutinin.—The macroscopic agglutination test was used with inactive serum and with killed bacterial suspension in normal salt solution. The mixtures were incubated at 37 C. for 2 hours and then placed in the icebox over night. The highest dilution of serum that agglutinated the bacteria was noted and was indicated by the figures recorded in tables 7 and 8.

Opsonin.—Opsonin was estimated by diluting the serum to the point of opsonic extinction, i. e., the dilution in which 50 leukocytes had the same number of cells taking part in phagocytosis as a normal control with salt solution. The points of opsonic extinction were noted as in table 9.

Hemolysin.—Antihuman hemolysin (table 1) was present in the blood of rabbit 1, 7 days before parturition in a 1:512 serum dilution. Immediately after the birth of the young, hemolysin was present in 1:256 dilution; it gradually decreased until it was 1:32, on the forty-first day after parturition. The blood of the young rabbit examined on the day of birth contained hemolysin in 1:128 dilution. As the young died on the day of birth, this was the only test made on the offspring. Antisheep hemolysin (table 2) was present in the blood of rabbit 2 in a 1:5,000 dilution, 1 day before it gave birth to its young. Six days after parturition its hemolysin titer was 1:640. It remained low until 38 days after parturition, when the rabbit developed an abscess. In a few days the titer again decreased, 1:80, and the rabbit died within a week. Hemolysin was present in all the young of the antisheep rabbit, but in lower titer than in the serum of the immunized mother. On the forty-fourth day all their serums contained hemolysin, and on the sixty-first day it was still demonstrable in 3 rabbits. Eighty days after birth, there was no trace of hemolysin in any of the offspring's serums. On the thirty-eight day, when the titer of the mother's serum rose to 1:1,280, there was no increase in the hemolysin titer of the young.

TABLE 1

ANTIHUMAN HEMOLYSIN (RABBIT 1)

Time	Serum		
	Mother	Offspring	Normal
7 days before birth	512	...	0
Day of birth	256	128	0
2 days after birth	256	...	0
4 days after birth	256	...	0
8 days after birth	128	...	0
11 days after birth	256	...	0
16 days after birth	256	...	0
20 days after birth	128	...	0
28 days after birth	64	...	0
37 days after birth	32	...	0
41 days after birth	32	...	0

TABLE 2

ANTISHEEP HEMOLYSIN (RABBIT 2)

Time	Serum						
	Mother	Offspring					Normal
		1	2	3	4	5	
1 day before birth	5,000	...	...	...	...	...	0
6 days after birth	640	...	160	...	...	...	0
11 days after birth	320	160	...	...	...	...	0
16 days after birth	160	80	40	40	80	40	0
21 days after birth	320	40	40	40	80	40	0
38 days after birth	1,280	20	10	40	20	40	0
44 days after birth	80	10	5	10	5	10	0
52 days after birth	dead	2	0	2	0	2	0
61 days after birth	.....	4	5	4	0	0	0
80 days after birth	.....	0	0	0	0	0	0

TABLE 3

COMPLEMENT FIXATION TEST WITH STREPTOCOCCUS VIRIDANS (RABBIT 3)

Time	Serum							
	Mother	Offspring						Normal
		1	2	3	4	5	6	
1 day before birth	++++	...	...	...	...	...	...	0
9 days after birth	0	0	...	...	...	...	...	0
11 days after birth	0	...	0	...	...	...	...	0
16 days after birth	0	...	...	0	...	...	...	0
19 days after birth	0	...	...	...	0	...	...	0
22 days after birth	+	...	...	...	...	0	...	0
30 days after birth	0	0	0	0	0	0	0	0
38 days after birth	0	+	0	0	+	+	+	0
52 days after birth	0	0	0	0	0	0	0	0
60 days after birth	0	0	0	0	0	0	0	0

TABLE 4

COMPLEMENT FIXATION TEST WITH PNEUMOCOCCUS (RABBIT 4)

Time	Serum		Offspring
	Mother	Normal	
1 day before birth	++++	0	Died
6 days after birth	0	0	
11 days after birth	+++	0	

TABLE 5

COMPLEMENT FIXATION TEST WITH MENINGOCOCCUS (RABBIT 5)

Time	Serum							
	Mother	Offspring						Normal
		1	2	3	4	5	6	
5 days before birth	++++	...	...	...	...	...	...	0
Day of birth	+	0	...	...	...	...	...	0
10 days after birth	++	...	0	...	...	...	...	0
16 days after birth	0	...	...	0	...	...	...	0
23 days after birth	+	...	...	...	0	...	...	0
33 days after birth	+	0	0	0	0	0	0	0

TABLE 6

COMPLEMENT FIXATION TEST WITH B. TYPHOSUS (RABBIT 6)

Time	Serum									
	Mother	Offspring								Normal
		1	2	3	4	5	6	7	8	
4 days before birth	++++	..	..	..	..	..	..	..	..	0
1 day after birth	++++	+++	..	..	..	..	..	..	..	0
8 days after birth	+++	..	++	..	..	..	..	..	..	0
14 days after birth	+++	..	..	+++	..	..	..	..	..	0
21 days after birth	+++	..	..	..	0	0	0	0	0	0
26 days after birth	0	0	0	0	0	0	0	0	0	0
32 days after birth	0	0	0	0	0	0	0	0	0	0

TABLE 7

AGGLUTININ FOR MENINGOCOCCUS (RABBIT 5)

Time	Serum							
	Mother	Offspring						Normal
		1	2	3	4	5	6	
5 days before birth	640	...	...	...	...	...	...	0
Day of birth	40	0	...	...	...	...	...	0
10 days after birth	320	...	40	...	...	...	...	0
16 days after birth	320	...	...	320	...	...	...	0
23 days after birth	10	...	...	...	160	...	...	0
33 days after birth	160	40	10	0	10	0	0	0

TABLE 8

AGGLUTININ FOR B. TYPHOSUS (RABBIT 6)

Time	Serum									
	Mother	Offspring								Normal
		1	2	3	4	5	6	7	8	
4 days before birth	1200	..	..	..	..	..	..	..	..	0
1 day after birth	1200	320	..	..	..	..	..	..	..	0
8 days after birth	1200	..	160	..	..	..	..	..	..	0
14 days after birth	320	..	..	160	..	..	..	..	..	0
21 days after birth	80	..	..	..	40	..	..	..	..	0
26 days after birth	80	10	20	10	80	40	10	10	10	0
32 days after birth	80	0	0	0	0	0	10	0	0	0

TABLE 9

OPSONIN FOR B. TYPHOSUS (RABBIT 6)

Time	Serum								
	Mother	Offspring							
		1	2	3	4	5	6	7	8
4 days before birth	640								
1 day after birth	20	20							
8 days after birth	40	..	40						
14 days after birth	40	..	..	20	20				
21 days after birth	80	..	..	..	..				
26 days after birth	40	20	20	10	10	10	20	20	20
32 days after birth	40	20	20	10	10	10	10	10	10

Complement-Fixation Antibodies.—Rabbit 3 (table 3) was immunized against Streptococcus viridans, and the serums of the immune mother and her offspring were tested for complement-fixation antibodies. The day before parturition the mother's serum gave complete inhibition of hemolysis in a streptococus fixation test. For 22 days after parturition no complement-fixing antibodies were demonstrable in either the mother's or in the offspring's blood. On the twenty-second day the mother's serum, and on the thirty-eighth day the serum of 4 of the young, slightly inhibited hemolysis. This was probably a non-specific reaction or was due to some error in technic. There was not enough serum to repeat the test.

Serum from rabbit 4 (table 4) immunized against a type 2 pneumococcus was also tested for complement-fixation antibodies. The serum gave a 4 plus fixation before the young were born and 6 days after birth a complete negative. When the rabbit's blood was tested again on the eleventh day, the complement-fixation reading was 3 plus. The young died on the day of birth.

Antimeningococcus complement-fixing antibodies were examined in the serum of rabbit 5 (table 5) and its offspring. Five days before parturition, the mother's serum gave a 4 plus fixation of complement, but on the day of birth only a 1 plus. The complement-fixation immune bodies remained low in the serum until the thirty-third day, when observation was discontinued. No demonstrable complement-fixation immune bodies were transmitted to the offspring of this rabbit.

Antityphoid complement-fixation antibodies were tested in rabbit 6 (table 6) and its young. Both before and after parturition the mother's serum gave complete inhibition of hemolysis in the typhoid complement-fixation test. The

titer for complement-fixation immune bodies remained high for 3 weeks, but on the twenty-sixth day it dropped to zero and remained there. Serum from the offspring of this rabbit had a high complement-fixing antibody content for 14 days after birth, but this entirely disappeared during the third week.

Agglutinin.—The agglutinin titer (table 7) was tested in the serum of the antimeningococcus rabbit (table 7) and in the serum of its offspring. There was a drop from 640 to 40 in the antimeningococcus rabbit serum after it gave birth to its young. The agglutinin content of the mother rabbit's serum fluctuated. On the thirty-third day, the last time it was examined, the titer was 1:160. The young rabbit examined on the day of birth had no demonstrable antimeningococcus agglutinin. On the sixteenth day the agglutinin titer was the same for the immunized rabbit and its young. On the thirty-third day 3 of the young rabbits had antimeningococcus agglutinin in their blood. The agglutinin content (table 8) of the serum of the antityphoid rabbit and its young was also examined. The agglutinin titer of the mother was high, 1:1,200, and remained at this point for 8 days after parturition. After this time it decreased rapidly, and on the twenty-first day it was only 1:80, at which point it remained until the thirty-second day, when the last examination was made. The serum of 1 of the offspring, examined a day after birth, contained antityphoid agglutinin in 1:320 serum dilution. All serums from the young contained agglutinin on the twenty-sixth day but on the thirty-second day only 1 serum contained agglutinin.

The serum of the antityphoid immune rabbit was examined for opsonin (table 9). Four days before parturition 1:640 serum dilution was the point of opsonic extinction, and 1 day after parturition the point of opsonic extinction had dropped to 1:20. The opsonic content of the serum remained low as long as the rabbit was under observation.. All the serums of the offspring contained opsonin (usually lower in quantity than in the mother), which persisted the 32 days in which the rabbits were observed.

SUMMARY

Antisheep and antihuman hemolysin was decreased in immunized rabbits after parturtition. The serum of their offspring contained hemolysin, but in lesser amounts than in the immune mother. There was little hemolysin in the serum of the young at the end of the sixth week and none at the end of the eleventh week.

Complement-fixing antibodies almost disappeared from the serum of 3 of the immune mothers (3, 4, 5) after parturition: In rabbit 3 there was no return of these immune bodies; in rabbit 5, only a slight increase of complement-fixing antibody; in rabbit 4, a return of the complement-fixing antibody. Rabbit 6 did not have an immediate loss of complement-fixing antibodies after parturition, but had marked decrease of these antibodies a week later. Complement-fixing antibodies could be determined in the offspring of rabbit 6 only, and were not present in these young rabbits after 2 weeks.

Agglutinin decreased in the serum of rabbit 5 and remained constant in rabbit 6 after parturition. Agglutinin was present in the

serum of the offspring (one exception—table 7) but in lesser amount than in the mother. The young of both immune mothers had a low agglutinin titer at the end of the fourth week.

The point of opsonic extinction in rabbit 6 fell from 640 to 20 after parturition. Opsonin remained low. The serums of the offspring had low points of opsonic extinction, but opsonin persisted after 5 weeks.

CONCLUSIONS

There is considerable variation in the antibody content in the serum of rabbits. The agglutinin and complement fixing antibodies appeared stable in the serum of rabbit 6 when they were compared with the immune bodies in other rabbits. Complement-fixing antibodies appear to be less stable than the other immune bodies studied and less readily transmitted to the young.

The results of these experiments do not indicate whether the young receive a passive immunity from the immune mother or whether they receive antibodies from the mother's milk. After parturition there was a marked decrease in the antibody content of the serum of the immunized rabbits, and this suggests a possible cause for the many post-partum infections. The offspring of immune rabbits, as a rule, have antibodies in their serum which persist in appreciable but decreasing amounts for 4 to 6 weeks.